UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,528	01/25/2001	Joseph A. Hedrick	DX0725K2B	7799

7590 02/13/2004

Sheela Mohan-Peterson, Esq.
DNAX Research Institute
901 California Avenue
Palo Alto, CA 94304-1104

EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

mailed 2-13-04

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040204

Application Number: 09/770,528
Filing Date: January 25, 2001
Appellant(s): HEDRICK ET AL.

Laurie L. Hill, Ph.D.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 01 December 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Appellant has indicated that there are no related appeals or interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is essentially correct. Two amendments after final were submitted by Appellant and were indicated as entered and considered by the examiner. These amendments were received on 16 October 2003 and 10 February 2003.

(5) Summary of Invention

The summary of invention contained in the brief is correct. Of course, the examiner respectfully disagrees with Appellant's conclusions that the claimed invention satisfies the requirements of 35 U.S.C. §§ 101 regarding utility and 112, first paragraph, regarding enablement, for the reasons set forth below.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 7-9 and 20-25 stand or fall together, that is, they can be considered as a single group.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,194,596	TISCHER ET AL.	3-1993
5,350,836	KOPCHICK ET AL.	9-1994

Murdoch et al., 2000, Blood 95:3032-3043.

Ji et al., 1998, J. Biol. Chem. 273:17299-17302.

Benjamin et al., 1998, Development 125:1591-1598.

Vukicevic et al., 1996, PNAS USA 93:9021-9026.

Massague, 1987, Cell 49:437-438.

Pilbeam et al., 1993, Bone 14:717-720.

Skolnick et al., 2000, Trends in Biotech. 18:34-39.

Bork, 2000, Genome Research 10:398-400.

Doerks et al., 1998, Trends in Genetics 14:248-250.

Smith et al., 1997, Nature Biotechnology 15:1222-1223.

Brenner, 1999, Trends in Genetics 15:132-133.

Bork et al., 1996, Trends in Genetics 12:425-427.

Debets et al., 2001, J. Immunol. 167:1440-1446.

Kumar et al., 2000, J. Biol. Chem. 275:10308-10314.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-9 and 20-25 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to binding compounds that bind amino acid sequences from the polypeptide of SEQ ID NO: 2, kits comprising same, compositions comprising same and methods of making antisera comprising the binding compounds. The utility of the recited binding compounds lies in the polypeptide (SEQ ID NO: 2) that the claimed binding compound binds. The specification asserts that the polypeptide of SEQ ID NO: 2 is a rodent IL-1δ polypeptide. "IL" is an abbreviation for "interleukin." The specification asserts that the invention has utility in that the IL-1δ is expected to have interleukin-1 like activities based on its structural similarity with known interleukins. For example, the specification asserts that IL-1δ can be used therapeutically for "a wide range of degenerative or abnormal conditions which directly or indirectly involve development, differentiation, or function, e.g., of the immune system and/or hematopoietic cells" (p. 3).

The assertion that the disclosed IL-1δ protein has biological activities similar to known IL-1 polypeptides cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. This is especially true for IL-1 polypeptides, as admitted in the specification at p. 3, lines 15-21, wherein it is stated that "[t]he interleukin-1 family of proteins includes the IL-1α, the IL-1β, the IL-1RA, and recently the IL-1γ (also designated Interferon-Gamma Inducing Factor, IGIF). This related family of genes have been implicated in a broad range of biological functions." See also pp. 31-32 of the specification. The IL-1 polypeptides bind different receptors (p. 41 of specification), indicating at least one mechanism by which these different IL-1 molecules exert different physiological effects. The instant specification does not disclose a specific receptor to which SEQ ID NO: 2 binds. Finally, note Kumar et al. (2000, J. Biol. Chem. 275:10308-10314) who disclose that IL-1δ is an antagonist of IL-1ε, even though both polypeptides belong to the IL-1 family.

Other cytokine or growth factor polypeptide families are also known in the art to have different biological activities, despite a close structural relationship. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences

between PDGF and VEGF are also seen in vivo, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). In the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF-β family (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48). Similarly, the receptors for cytokines and growth factors share structural similarity, but have diverse activities and physiological effects. For example, Murdoch et al. (2000, Blood 95:3032-3043) review chemokine receptors, which are structurally similar and yet are expressed on different cell types and bind different ligands such that the receptor response is highly variable (p. 3032, Abstract). Ji et al. (1998, Journal of Biological Chemistry 273:17299-17302) review the functional diversity among the structurally related G protein-coupled receptors.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a

small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality for new members of cytokine or growth factor polypeptide families, the assertion that the IL-1δ polypeptide recited in the claims has activities similar to previously characterized IL-1 polypeptides is not substantial. Significant further research would have been required of the skilled artisan to characterize the polypeptide of SEQ ID NO: 2 to determine its particular biological activities or other specific utilities.

In view of the evidence in the art that structural similarity between soluble polypeptides like interleukins, as well as other cytokines and growth factors, cannot accurately predict functional similarity, there is also no well-established utility for newly isolated IL-1δ or the claimed binding compounds.

The specification asserts several utilities for IL-1δ that are not necessarily related to its biological activities; however, none of these asserted utilities meets the three-pronged test of being credible, specific and substantial. Each will be addressed in turn:

a) *IL-1δ or its binding compounds can be used in therapy:* This asserted utility is credible, but it is not specific or substantial. In particular, the specification states at pp. 79-80 that IL-1δ "likely play[s] a role in modulating of local and systemic inflammatory processes", but does not state what the role is, what types of inflammation involve IL-1δ, or how IL-1δ modulates the inflammation. The specification provides no clear nexus

between any particular inflammatory state and any specific change in IL-1δ form or quantity. Since significant further research would be required before IL-1δ could be used in a real-world treatment of a specific disease, the asserted utility is not substantial. Also, a diverse group of chemical and environmental stimuli can be said to "play a role in modulating of local and systemic inflammatory processes", including cytokines, aspirin, lye, scratches, and ice. Some of these enhance inflammation (e.g., certain cytokines, lye, scratches) whereas others relieve inflammation (e.g., other cytokines, aspirin, ice). However, all of these diverse stimuli can be said to "modulate" or "play a role" in inflammation. Therefore, the assertion that Il-1δ plays a role in modulating inflammation is not a specific assertion of utility.

b) *IL-1δ can be used to screen for receptors, agonists or antagonists:* This asserted utility is credible and substantial, but it is not specific. The same can be done with any structurally and functionally unrelated polypeptide.

c) *IL-1δ can be used as a disease marker or as a tissue marker:* The specification does not provide a nexus between any particular disease state and an alteration in forms or levels of IL-1δ. Again, the specification asserts that IL-1δ "likely play[s] a role in modulating of local and systemic inflammatory processes", and does not state what the role is, what types of inflammation involve IL-1δ, or how IL-1δ forms or levels are changed in inflamed tissues. Therefore, the assertion that IL-1δ can be used as an inflammation disease marker is credible, but it is not specific or substantial. Significant further research would be required to discover the nexus between a particular disease state and a particular alteration in IL-1δ forms or levels. Use as a

tissue marker is credible, but it is not specific. Numerous structurally and functionally unrelated proteins can be used as tissue markers based on their expression patterns. This asserted utility is also not substantial since the tissue specific pattern of expression for SEQ ID NO: 2 was not disclosed in the specification, and would have to be determined empirically by the skilled artisan.

d) IL-1δ can be used to make antibodies, and the antibodies can be used to identify IL-1δ: This asserted utility is credible, but not specific or substantial. Antibodies can be made from any protein. Also, there is no indication of how to use the antibodies in a real-world use.

Therefore, since the specification does not disclose a specific, substantial and credible utility for the claimed binding compounds or the polypeptide they bind, the claims are rejected under 35 U.S.C. § 101 for lack of utility.

Claims 7-9 and 20-25 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

Appellant argues that the specification asserts a specific, substantial and credible utility for a binding compounds specific for IL-1δ. At p. 5, first paragraph, Appellant

reviews the Office's arguments and asserts that the rejection is in error. Appellant's specific arguments are divided into five parts.

A) Legal standard of the utility requirement: Referring to the M.P.E.P., Appellant reviews the legal standard of the utility requirement. Appellant states that the Office has taken the legally incorrect position that only certain evidence substantiated by actual experimental data would establish patentable utilities. This has been fully considered but is not found to be persuasive. The Office Actions have not required particular evidence or experimental data. The Office Actions have provided an analysis of the disclosure and additional evidence submitted by Appellant, and set forth the findings that the totality of the disclosure and evidence do not meet the requirements of 35 U.S.C. § 101 for a credible, specific and substantial asserted utility or a well-established utility, as discussed in the rejection above.

Appellant urges that a disclosed utility for the claimed subject matter satisfies the utility requirement absent evidence which would cast doubt on the objective truth of the disclosed utility, and that there is no legal requirement that the disclosed utility must be supported by conclusive experimental data. Appellant urges that evidence is only required if the skilled artisan would conclude that the asserted utility is more likely than not true. For pharmaceutical utilities, Appellant urges that only a reasonable correlation between the evidence and the asserted utility is sufficient. Finally, Appellant states that the courts have routinely found evidence of structural similarity to a compound known to have a particular therapeutic utility as being supportive of an assertion of therapeutic utility for a new compound. This has been fully considered. The examiner takes no

issue with Appellant's discussion of the legal requirements of 35 U.S.C. § 101. It is respectfully pointed out that the Office Actions have never brought into question the credibility of the asserted utilities. However, an asserted utility must meet the three-pronged test of being credible, specific and substantial. As discussed in the rejection set forth above, none of the asserted utilities satisfy all three prongs. Furthermore, whereas the courts have routinely found evidence of structural similarity to a compound known to have a therapeutic utility as being supportive of an assertion of therapeutic utility for a new compound, this is not a *per se* rule. This is only true when there is no evidence that members of a class of structurally similar compounds have diverse functions. The Office Actions have brought forth evidence that cytokines generally, and interleukin-1 polypeptides particularly, are structurally similar and yet functionally diverse. See Tischer et al., Kopchick et al., Murdoch et al., Ji et al., Benjamin et al., Vukicevic et al., Massague, Pilbeam et al., Skolnick et al., Bork, 2000, Doerks et al., Smith et al., Brenner, and Bork et al., 1996, of record. See also pp. 3 and 31-32 of the specification which admits that interleukin-1 polypeptides are functionally diverse, and p. 41 which admits that the different interleukin-1 polypeptides bind different receptors. See also Kumar et al., who disclose that IL-1δ is an antagonist of IL-1ε. In the face of this evidence, the skilled artisan would not accept the assertion that a new interleukin-1 has functions similar to other interleukin-1 polypeptides. The skilled artisan would have to conduct significant further research to determine the particular functions of the new interleukin-1 in order to identify a credible, specific and substantial utility for the new interleukin-1. In such a case, the asserted utility is not substantial.

Appellant argues that only one credible assertion of specific utility is required to satisfy the requirements of 35 U.S.C. § 101. Appellant also urges that additional statements of utility, even if not credible, do not render the claimed invention lacking in utility. The examiner agrees that only one assertion of a credible, specific and substantial utility needs to be present in the specification. However, for the reasons set forth in the rejection above, none of the asserted utilities in the specification satisfies the three-pronged test for utility: credible, specific and substantial.

Appellant argues that an assertion of utility is credible unless the logic underlying the assertion is seriously flawed. This is true; however, the credibility of any utility asserted in the specification has not been questioned.

Appellant argues that the Office has adopted an incorrect standard by requiring certain and exact evidence, i.e., that the specification state that IL-1δ is upregulated in psoriasis. Appellant argues that the Office is requiring proof beyond a reasonable doubt regarding the role of IL-1δ in inflammation and immune responses. This has been fully considered but is not found to be persuasive. Given the disclosure of Debets et al., a post-filing date reference of record, there is no doubt that IL-1δ is over-expressed in psoriasis, a particular type of inflammation. However, the specification as originally filed merely states that IL-1δ is likely to "play a role" in inflammation. There is no disclosure suggesting what type of role is played, nor what types of inflammation involve IL-1δ. The asserted utility of "likely to play a role in inflammation" is not substantial. It would have taken significant research, exactly what Debets et al. did, to determine that one of IL-1δ's "roles" is up-regulation in tissues with psoriasis.

B) IL-1δ has a specific utility: Beginning at p. 7, Appellant argues that the specification's disclosure of a utility for IL-δ as a cytokine with a role in inflammation is specific. Appellant argues that inflammation is a specific disease characterized by a complex response, as outlined in the second full paragraph of p. 7 of the Brief. Appellant argues that the diversity of the resulting disease states is specific to the organ system in which the inflammation occurs, not the initiation inflammatory process. Appellant urges that the identification of inflammation as a specific pathological response in which IL-1δ plays a role is a specific assertion of utility for IL-1δ. This has been fully considered but is not found to be persuasive. The specification states that at pp. 79-80 that IL-1δ "likely play[s] a role in modulating of local and systemic inflammatory processes." A diverse group of chemical and environmental stimuli can be said to "play a role in modulating of local and systemic inflammatory reactions," including cytokines, aspirin, lye, scratches, and ice. Some of these enhance inflammation (e.g., certain cytokines, lye, scratches) whereas others relieve inflammation (e.g., other cytokines, aspirin, ice). However, all of these diverse stimuli can be said to "modulate" or "play a role" in inflammation. Therefore, the assertion that Il-1δ plays a role in modulating inflammation is not a specific assertion of utility.

Also, the specification does not state what IL-1δ's role in inflammation is, what types of inflammation involve IL-1δ, or how IL-1δ modulates the inflammation. The specification provides no clear nexus between any particular inflammatory state and any specific change in IL-1δ form or quantity. Since significant further research would be required

before IL-1d could be used in a real-world treatment of a specific disease, the asserted utility is not substantial.

Appellant argues that there is no requirement to predict the specific effects of IL-1δ in inflammation, as there is no predetermined amount or character of evidence needed to support an asserted utility. Appellant argues that the threshold of utility is not high under 35 U.S.C. § 101. Citing case law, Appellant asserts that an invention is useful if it is merely capable of providing some identifiable benefit, i.e., a minimal utility. Appellant argues that the character and amount of evidence required is determined by what is claimed and whether it contravenes established scientific principal and belief. This has been fully considered but is not found to be persuasive. The asserted utility at issue is that Il-1δ "likely play[s] a role in modulating of local and systemic inflammatory processes". The credibility of this assertion is not brought into question. Most cytokines play a role in inflammation. However, this information does not provide the skilled artisan with an identifiable benefit, or a minimal utility. What can the skilled artisan do with IL-1δ armed only with the assertion that it plays a role in modulating inflammation? Does the skilled artisan administer it to inflamed tissue or, conversely, try to inhibit it in the inflamed tissue? Would there be any effect in inflamed pancreas tissue, or inflamed gastrointestinal lining, or allergic inflammation? The specification provides no clear nexus between any particular inflammatory state and any specific change in IL-1δ form or quantity, and thus it is up to the skilled artisan to determine such by empirical experimentation. Since significant further research would be required before IL-1δ could be used in a real-world treatment or diagnosis of a specific disease, the asserted

utility is not substantial. Also, since inflammation is "modulated" by a diverse group of chemical and environmental stimuli that "play a role", the asserted utility at issue is not specific.

Appellant argues that the specification discloses a specific cytokine, IL-1δ, and asserts a specific biological activity for it as a modulator of at least one specific disease, namely inflammation. Appellant explains that the character of the evidence supporting this utility lies in the structural similarities between IL-1δ and other family members, as outlined in the third paragraph of p. 8 of the Brief. Appellant argues that all of the IL-1 family members that have been functionally characterized are involved in inflammation, and thus the specification discloses that IL-1δ affects inflammatory responses. This has been fully considered but is not found to be persuasive. There is little doubt that IL-1δ is a new member of the IL-1 family of cytokines, and that all of the IL-1 polypeptides characterized to date play a role of some sort in inflammation. However, these roles are diverse. For example, IL-1δ is an antagonist of IL-1ε as disclosed by Kumar et al. Appellant refers to p. 31 of the specification. What is disclosed there is, "IL-1δ and IL-1ε and their agonists or antagonists should have related activities, typically affecting similar immune functions, including inflammatory responses." However, post-filing date disclosures such as Kumar et al. do not support the specification's statements that IL-1δ and IL-1εhave similar activities. Also, the specification admits at p. 3, lines 15-21, "[t]he interleukin-1 family of proteins includes the IL-1α, the IL-1β, the IL-1RA, and recently the IL-1γ (also designated Interferon-Gamma Inducing Factor, IGIF). This related family of genes have been implicated in a broad range of biological functions." See also pp. 31-

32 of the specification. The IL-1 polypeptides bind different receptors (p. 41 of specification), indicating at least one mechanism by which these different IL-1 molecules exert different physiological effects. The instant specification does not disclose a specific receptor to which SEQ ID NO: 2 binds, nor any information specific to IL-1δ among the other IL-1 polypeptides or, indeed, any number of other cytokines.

Appellant reviews the post-filing date references brought forth as evidence in this case. First, Appellant reviews the findings of Debets et al. (2001, of record) in the paragraph bridging pp. 8-9 of the Brief. Appellant concludes that Debets et al. provide evidence of the role of IL-1δ in inflammation. Appellant also reviews the disclosure of Kumar et al. (2000, of record) at the second paragraph of p. 9 of the Brief. Appellant concludes that Kumar et al. further support a specific utility for IL-1δ as a modulator of inflammation through its ability to act as an antagonist of IL-1ε. This has been fully considered but is not found to be persuasive. The assertion in the specification that IL-1δ is likely to play a role in the modulation of inflammation is not a specific assertion of utility. A very diverse number of compounds and environmental stimuli play a role in modulation of inflammation. The post-filing date references of Debets et al. and Kumar et al. constitute specific disclosures of what IL-1δ's role in inflammation is. Unfortunately, these specific roles are not asserted in the specification as originally filed.

Appellant argues that the asserted utility does not contravene scientific principle and belief. The examiner takes no issue with the credibility of the asserted utility. The issue is not that the assertion of utility is not credible, rather, the issue is that the

assertion that IL-1δ is likely to play a role in the modulation of inflammation is not specific or substantial.

Appellant argues that the fact that diverse compounds elicit an inflammatory response is not relevant to the specific utility of IL-1δ in inflammation. Appellant argues that lye, a scratch, aspirin and ice are not comparable to IL-1δ in that they require no specific biological interaction (such as those involving keratinocytes, other cytokines or psoriasis) to mediate any of their effects in inflammation. This has been fully considered and is interpreted to support the Office Actions' findings. The specification only asserts a very non-specific role of IL-1δ in inflammation, in particular, that IL-1δ "likely play[s] a role in modulating of local and systemic inflammatory processes". That is exactly what lye, a scratch, aspirin or ice do. The specific biological interactions that occur during inflammation, as mentioned in Appellant's arguments and at pp. 79-80 of the specification, are inherently part of the inflammatory response. If the specification had asserted that IL-1δ is up-regulated in psoriasis, or is elicited in keratinocytes but not other cells, then the assertion of utility would have been found to be specific. Unfortunately, that is not what is in the specification as originally filed.

Appellant disagrees with the Office's assertion that the literature does not support the specification's more specific assertions of the effects of IL-1δ. Appellant characterizes the Office's list of effects as a limited laundry list of the characteristics of the inflammatory response. Appellant argues that the literature submitted by Appellant do not examine these characteristics. Appellant concludes that the evidence of record is sufficiently probative regarding the expression of IL-1δ during inflammatory responses

and diseases, and the modulation of the binding of IL-1ε to establish the specific utility of IL-1δ. This has been fully considered but is not found to be persuasive. It appears that Appellant is addressing the Office Action of 12 August 2003 at p. 3, wherein it was stated that the literature does not support the specification's more specific assertions of the effects of IL-1δ (e.g., it induces chemoattractants, it enhances and promotes adherence of adhesion molecules resulting in recruitment of macrophages/neutrophils, it induces fibroblast growth, etc., as discussed at pp. 79-80 of the specification). The Office Action's discussion of these more specific assertions was presented to show that the Debets et al. and Kumar et al. references were considered in their entirety. The specification asserts some specific activities for IL-1δ as listed above, based on IL-1δ's structural similarity to other IL-1 polypeptides. However, as argued on the record, that assertion cannot be accepted in the absence of supporting evidence because the IL-1 family of polypeptides is functionally diverse, as admitted in the specification. Perhaps the most clear evidence of the functional diversity of the IL-1 family members is Kumar et al.'s disclosure that IL-1δ is an antagonist of IL-1ε. In any case, neither Debets et al. nor Kumar et al. supported any of the specification's more specific assertions of activities relative to the inflammatory process.

C) IL-1δ has a substantial utility: Beginning at the bottom of p. 10 of the Brief, Appellant argues that the assertion of a utility for IL-1δ in inflammation satisfies the substantiality prong for the utility requirement. Appellant quotes the M.P.E.P. regarding the courts having repeatedly found that the mere identification of a pharmacological activity of a compound is relevant to an asserted pharmacological use provides an

immediate benefit to the public. Appellant urges that the specification's identification of IL-1δ as having a role in inflammation and as an inhibitor of IL-1ε provides researchers and physicians with a new target for intervention in inflammatory responses and diseases. Appellant argues that an antibody that binds IL-1δ has a real world use because the ability to measure the presence of IL-1δ in inflammation permits diagnosis of inflammation and the identification of potential pharmacological agents for preventative measures or monitoring of disease progression. This has been fully considered but is not found to be persuasive. It is true that the identification of a pharmacological activity is substantial, however, the specification does not assert a pharmacological activity for IL-1δ. The specification merely states that IL-1δ is likely to play a role in modulating inflammation. It does not characterize that role. Therefore, the skilled artisan must conduct further experiments to determine the role of IL-1δ in inflammation. Is it up-regulated or down-regulated during inflammation? Without this information, the skilled artisan would not know if it was desirable to identify drugs that agonize or antagonize IL-1δ as a treatment for inflammation. Does IL-1 play a role in skin inflammation or pancreas inflammation, or inflammation of any other tissue? Without this information, the skilled artisan would have to conduct experiments to identify specific inflammatory responses that involve IL-1δ. Thus, the specification's assertion that IL-1δ is likely to play a role in the modulation of inflammation is not substantial. Also, the specification does not assert that IL-1δ is an antagonist of IL-1ε. This was disclosed in Kumar et al. However, even if the specification had asserted that IL-1δ is an antagonist of IL-1ε, this would still not be considered a substantial assertion

of utility, because neither IL-1δ nor IL-1ε were disclosed in the specification as having a specific and substantial utility.

D) IL-1δ has a credible utility: Beginning at p. 11 of the Brief, Appellant argues that IL-1δ has a credible utility, as asserted in the specification that IL-1δ plays a role in inflammation. This has been fully considered. The credibility of the specification's assertion that IL-1δ plays a role in inflammation has never been brought into question. Many diverse compounds and environmental stimuli play a role in inflammation, and thus the assertion is credible on its face. However, as argued above, the assertion is not specific or substantial, and thus the claimed invention lacks utility.

E) The specification discloses additional utilities for IL-1δ: Beginning at the bottom of p. 11 of the Brief, Appellant argues that the specification sets forth other specific, substantial and credible utilities for IL-1δ, namely, that IL-1δ is involved in viral infections and immunological disorders (pp. 78-79 of the specification). This has been fully considered but is not found to be persuasive. At pp. 78-79, the specification states,

> "This invention provides reagents with significant therapeutic value. The IL-1δ or IL-1ε (naturally occurring or recombinant), fragments thereof, muteins agonists and antagonists, and antibodies, along with compounds identified as having binding affinity to the interleukin or its receptor or antibodies, should be useful in the treatment of conditions exhibiting abnormal expression of the interleukin. Such abnormality will typically be manifested by immunological disorders. Additionally, this invention should provide therapeutic value in various diseases or disorders associated with abnormal expression or abnormal triggering of response to the interleukin. The mouse IL-γ has been suggested to be involved in tumors, allergies, and infectious diseases, e.g., pulmonary tuberculosis, leprosy, culminant hepatitis, and viral infections, such as HIV. The IL-1δ and/or IL-1ε or antagonist may have similar function."

Again, these assertions are not specific or substantial, since many diverse compounds and environmental stimuli *or their antagonists*, can be used in such treatments. Also, the specification does not specify whether the interleukins *or* their antagonists should be administered. The skilled artisan must conduct further experiments to determine what role, if any, IL-1δ plays in any of these diseases, and then determine whether or not administration of IL-1δ or its antagonist would be beneficial. Even then, the role of IL-1δ may be so minimal that targeting IL-1δ with a drug may not affect the overall inflammation. Clearly, the asserted utility is not substantial.

Appellant points to Debets et al. and Kumar et al. as specifically supporting the specification's assertions that IL-1δ is involved in viral infections and immunological disorders in their disclosures that IL-1δ acts as an antagonist of IL-1ε and thus can modulate the immune response mediated by IL-1ε. Appellant argues that the specification discloses that IL-1δ and IL-1ε have related activities in immune functions at p. 31. Appellant reasons that IL-1ε and IL-1δ regulate a single signaling cascade as agonist and antagonist. This has been fully considered but is not found to be persuasive. Appellant refers to the disclosures of Kumar et al. and Debets et al., but their disclosure that IL-1δ is an antagonist of IL-1ε is not found in the specification as originally filed. The requirements of 35 U.S.C. § 101 regarding utility is that, in the absence of a well-established utility, the *specification* must assert a credible, specific and substantial utility for the claimed invention. The requirement is *not* that the *post-filing date references* assert a credible, specific and substantial utility. The specification does not state that IL-1δ is an antagonist of IL-1ε. However, even if the specification did

assert this, there are no specific and substantial assertions of utility for IL-1δ or IL-1ε and so the information that there is an antagonist relationship does not constitute a specific or substantial assertion of utility in and of itself. Appellant refers to p. 31 of the specification. There it is stated, "IL-1δ and IL-1ε and their agonists or antagonists should have related activities, typically affecting similar immune functions, including inflammatory responses." Thus, the specification implies that IL-1δ and IL-1ε have similar activities, not an antagonistic relationship.

Appellant refers to Kumar et al. as disclosing that IL-1ε is expressed in response to herpes simplex viral infection. Appellant argues that IL-1ε functions similarly to IL-1α and IL-1β in its involvement in viral response, while IL-1δ functions to IL-1RA as a modulator of particular IL-1 family members. Appellant concludes that the references thus support an additional disclosed utility for IL-1δ as a modulator of immune responses, particularly in anti-viral infections. This has been fully considered but is not found to be persuasive, since none of these specific interactions is disclosed in the specification as originally filed. Again, 35 U.S.C. § 101 requires that, in the absence of a well-established utility, the *specification* must provide an assertion of a credible, specific and substantial utility. Whereas a post-filing date reference may be used to support such an assertion made in the specification, it cannot take the place of the assertion itself.

In conclusion, the specification fails to provide an assertion of a credible, specific and substantial utility for the claimed binding compounds or the polypeptide they bind, and there is no well-established utility for a new interleukin-1 since the interleukin-1

family is known for its functional diversity. It is clear from the instant specification that the IL-1δ polypeptide described therein is what is a new interleukin-1 polypeptide which was isolated because of its similarity to known interleukin-1 polypeptides. Debets et al. and Kumar et al. provide further characterization of the IL-1δ protein which provide a credible, specific and substantial utility for IL-1δ. This further characterization, however, is part of the act of invention and until it was undertaken, Appellant's claimed invention as disclosed in the specification as originally filed, was incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Elizabeth C. Kemmerer, Ph.D.
February 9, 2004

Conferees
Yvonne Eyler, Ph.D.
Gary Kunz, Ph.D.

Gary Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Sheela Mohan-Peterson, Esq.
DNAX Research Institute
901 California Avenue
Palo Alto, CA 94304-1104

Yvonne Eyler

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600